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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/800,541	03/07/2001	Liselotte Bjerre Knudsen	6169.200-US	4130

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EXAMINER
ROMEO, DAVID S

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 02/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09.800,541	KNUDSEN, LISELOTTE BJERRE
	Examiner	Art Unit
	David S Romeo	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-42* is/are pending in the application.

4a) Of the above claim(s) *30-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-29 and 36-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *26-42* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other .

DETAILED ACTION

Claims 26-42 are pending.

Applicant's election of group I, claims 26-29, 36-42, and the species Arg^{34},Lys^{26}(N^{ε}-γ-Glu(N^{α}-hexadecanoyl)))GLP-1(7-37) in Paper No. 10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 30-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 10.

The application is not fully in compliance with the sequence rules, 37 C.F.R. § 1.821-1.825. Specifically, the specification fails to recite the appropriate sequence identifiers at each place where a sequence is discussed. See, for example, page 12, lines 21-31. This is not meant to be an exhaustive list of places where the specification fails to comply with the sequence rules. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. The application cannot issue until it is in compliance. Nucleic acid sequences with 10 or more nucleotides, at least 4 of which are specifically defined, must comply with the sequence rules. Amino acid sequences with 4 or more residues, at least 4 of which are specifically defined, must comply with the sequence rules.

Sequence identifiers can also be used to discuss and or claim parts or fragments of a properly presented sequence. For example, language such as "residues 14 to 243 of SEQ ID NO:23" is permissible and the fragment need not be separately presented in the "Sequence Listing."

Correction is required.

Inventorship

In view of the papers filed March 12, 2002 (Paper No. 8), it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by adding Johan Selmer, Jeppe Sturis, and Philip Just Larsen as inventors.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 26, 27, 36, 37, 40 are rejected under 35 U.S.C. 102(a) as being anticipated by Banchovin (1, cited by Applicants) in view of Howard (v11). Banchovin teaches that

hyperlipoproteinemia is a complication of diabetes. The cumulative effect of these diabetes-associated abnormalities is severe blood vessel and nerve damage. See page 2, full paragraph 1. Banchovin provides improved methods for reducing hyperlipidemia and/or hyperlipoproteinemia and for abating atherosclerosis (page 3, lines 29-31) and methods for producing beneficial changes in blood lipoprotein levels, and thus to provide effective treatments for diabetes, obesity and/or atherosclerosis (page 4, full paragraph 3). The method includes the administration of an inhibitor which inhibits the proteolysis of GLP-1 and accordingly increases the plasma half-life of GLP-1 (page 5, last full paragraph). Accordingly, these inhibitors are GLP-1 agonist. The inhibitors possess the ability to lower blood lipid levels. They are thus useful for the therapy of hyperlipidemia and diabetic complications (including coronary artery disease and arteriosclerosis). See page 28, last full paragraph. Essentially any and/or all patients, including diabetic and/or obese patients, including such patients with or without cardiovascular disease, are in need of such treatment because such treatment lowers the risk of cardiovascular disease in accordance with the present specification at page 2, full paragraph 2. The examiner uses the present specification as a definition of the term "patient in need of such treatment". Howard teaches that the cornerstone of therapy for diabetic patients should essentially consider the management of dyslipidemia along with the hyperglycemia, hypertension, and obesity (page 219, left column). An understanding of lipoprotein metabolism in diabetes is essential because dyslipidemia contributes to the atherosclerotic process in diabetic individual (page 216, Abstract). The leading cause of death for individuals with diabetes is cardiovascular disease, and one of the most important factors that contribute to this is the alteration in lipoproteins that occur in diabetic subjects (page 216, left column, "Introduction").

Claims 26-29, 36-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Eng (a11) in view of Raufman (u11) and in view of Howard (v11). Eng discloses pharmaceutical compositions containing exendin-3 or exendin-4, or any combination thereof, and methods for the treatment of diabetes mellitus and the prevention of hyperglycemia (column 2, lines 35-40). Essentially any and/or all patients, including diabetic and/or obese patients, including such patients with or without cardiovascular disease, are in need of such treatment because such treatment lowers the risk of cardiovascular disease in accordance with the present specification at page 2, full paragraph 2. The examiner uses the present specification as a definition of the term "patient in need of such treatment". Howard teaches that the cornerstone of therapy for diabetic patients should essentially consider the management of dyslipidemia along with the hyperglycemia, hypertension, and obesity (page 219, left column). An understanding of lipoprotein metabolism in diabetes is essential because dyslipidemia contributes to the atherosclerotic process in diabetic individual (page 216, Abstract). The leading cause of death for individuals with diabetes is cardiovascular disease, and one of the most important factors that contribute to this is the alteration in lipoproteins that occur in diabetic subjects (page 216, left column, "Introduction"). GLP-1(7-36) interacts with exendin receptors. See Raufman, page 21432, right column, last full paragraph. Accordingly, an exendin receptor is a GLP-1 receptor. Exendin-3 or -4 binds a GLP-1 receptor with an affinity constant below 1 μM in the absence of evidence to the contrary. Burden is shifted to applicant to distinguish Applicant's invention from Eng's invention.

Claims 26, 27, 29, 36, 37, 39, 40, 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Efendic (b11) in view of Howard (v11). Efendic discloses infusing GLP-1 (7-36)amide at a rate of 0.75 pmol per kilogram of body weight per minute in insulin treated obese NIDDM patients (paragraph bridging columns 5-6). Essentially any and/or all patients, including diabetic and/or obese patients, including such patients with or without cardiovascular disease, are in need of such treatment because such treatment lowers the risk of cardiovascular disease in accordance with the present specification at page 2, full paragraph 2. The examiner uses the present specification as a definition of the term "patient in need of such treatment". Howard teaches that the cornerstone of therapy for diabetic patients should essentially consider the management of dyslipidemia along with the hyperglycemia, hypertension, and obesity (page 219, left column). An understanding of lipoprotein metabolism in diabetes is essential because dyslipidemia contributes to the atherosclerotic process in diabetic individual (page 216, Abstract). The leading cause of death for individuals with diabetes is cardiovascular disease, and one of the most important factors that contribute to this is the alteration in lipoproteins that occur in diabetic subjects (page 216, left column, "Introduction"). It is reasonable to assume that GLP-1 (7-36)amide binds a GLP-1 receptor with an affinity constant below 1 μM in the absence of evidence to the contrary. Burden is shifted to applicant to distinguish Applicant's invention from Efendic.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

> pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26-29, 36-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of lowering plasma levels of triglycerides, free fatty acids, or total cholesterol, does not reasonably provide enablement for a method of lowering one or more serum lipids, of reducing the serum LDL:HDL ratio, or of reducing the serum level of lp(A) or apo(A). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The specification envisions lowering one or more serum lipids, reducing the serum LDL:HDL ratio, and reducing the serum level of lp(A) or apo(A). The only working examples in the specification show lowering plasma levels of triglycerides, free fatty acids, or total cholesterol. The claims are directed to or encompass lowering one or more serum lipids, reducing the serum LDL:HDL ratio, and reducing the serum level of lp(A) or apo(A). However, no changes were observed in the levels of LDL and HDL cholesterol after administration of GLP-1. See Juniti-Berggren (3, cited by Applicants), page 1200, "RESULTS". This is objective evidence that the full scope of the claims is not enabled. No guidance for, or working examples of, practicing the invention commensurate with the full scope of the claims is provided. The skilled artisan is left to unduly extensive experimentation involving random, trial and error, and fundamentally unpredictable experimentation.

Claims 26-29, 36-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification envisions lowering one or more serum lipids, reducing the serum LDL:HDL ratio, and reducing the serum level of lp(A) or apo(A). The only working examples in the specification show lowering plasma levels of triglycerides, free fatty acids, or total cholesterol. The claims are directed to or encompass lowering one or more serum lipids, reducing the serum LDL:HDL ratio, and reducing the serum level of lp(A) or apo(A). However, no changes were observed in the levels of LDL and HDL cholesterol after administration of GLP-1. See Juniti-Berggren (3, cited by Applicants), page 1200, "RESULTS". This is objective evidence that the full scope of the claims is not described. No specific guidance for, or working examples of, practicing the invention commensurate with the full scope of the claims is described.

Claims 26, 27, 29, 36, 37, 39, 40, 42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to or encompass a GLP-1 agonist. The term "GLP-1 agonist" is a genus of compounds. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any structural limitations on the structure of the agonist. Thus, the scope of the claim includes numerous structural variants, and the genus is

highly variant because there are no structural limitations to the genus. See, for example, the GLP-1 agonists compounds of Banchovin (1, cited by Applicants). Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Although it might be obvious for the skilled artisan to screen for compounds with GLP-1 agonist activity, the written description requirement is not satisfied by that which is obvious over what is disclosed; it is satisfied by that which is disclosed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the specific structural analogs of GLP-1 disclosed in the preset specification, alone are insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 26-29, 36-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 39, 40 of U.S. Patent No. 6,268,343 (c11) in view of Howard (v11) and Efendic (b11). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of set of claims is directed to or encompasses the administration of Arg^{34},Lys^{26}(N^{ε}-γ-Glu(N^{α}-hexadecanoyl)))GLP-1(7-37) for the treatment of diabetes or obesity. Essentially any and/or all patients, including diabetic and/or obese patients, including such patients with or without cardiovascular disease, are in need of such treatment because such treatment lowers the risk of cardiovascular disease in accordance with the present specification at page 2, full paragraph 2. The examiner uses the present specification as a definition of the term "patient in need of such treatment". Howard teaches that the cornerstone of therapy for diabetic patients should essentially consider the management of dyslipidemia along with the hyperglycemia, hypertension, and obesity (page 219, left column). An understanding of lipoprotein metabolism in diabetes is essential because dyslipidemia contributes to the atherosclerotic process in diabetic individual (page 216, Abstract). The leading cause of death for individuals with diabetes is cardiovascular disease, and one of the most important factors that contribute to this is the alteration in lipoproteins that occur in diabetic subjects (page 216, left column, "Introduction"). Diabetic patients can also be obese patients, as evidenced by Efendic (paragraph bridging columns 5-6).

Claims 26-29, 36-42 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19, 20 of copending Application No. 6,458,924 (d11) in view of Howard (v11) and Efendic (b11). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of set of claims is directed to or encompasses the administration of Arg^{34},Lys^{26}(N^{ε}-γ-Glu(N^{α}-hexadecanoyl)))GLP-1(7-37) for the treatment of diabetes or obesity. Essentially any and/or all patients, including diabetic and/or obese patients, including such patients with or without cardiovascular disease, are in need of such treatment because such treatment lowers the risk of cardiovascular disease in accordance with the present specification at page 2, full paragraph 2. The examiner uses the present specification as a definition of the term "patient in need of such treatment". Howard teaches that the cornerstone of therapy for diabetic patients should essentially consider the management of dyslipidemia along with the hyperglycemia, hypertension, and obesity (page 219, left column). An understanding of lipoprotein metabolism in diabetes is essential because dyslipidemia contributes to the atherosclerotic process in diabetic individual (page 216, Abstract). The leading cause of death for individuals with diabetes is cardiovascular disease, and one of the most important factors that contribute to this is the alteration in lipoproteins that occur in diabetic subjects (page 216, left column, "Introduction"). Diabetic patients can also be obese patients, as evidenced by Efendic (paragraph bridging columns 5-6).

Conclusion

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

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FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

David Romeo

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
FEBRUARY 23, 2003